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We proposed to examine the novel hypothesis that the hCG genotype of a woman's offspring is associated with her breast cancer risk. Using the existing Metropolitan New York Registry (MNYR) resources, a case-control study was designed to examine the hypothesis whether first-born offspring's hCGβ 5 genotype (i.e., placental hCGβ 5 genotype during first FTP) is associated with a woman's breast cancer risk. To date, the three tasks in the approved Statement of Work for year 1 have been accomplished.

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Table of Contents

INTRODUCTION:

It has long been known that both early age at first birth and total number of full-term pregnancies (FTPs) reduce breast cancer risk[1-5]. The underlying biology of this protection is yet to be clearly known. One or more of the hormonal changes during pregnancy are the logical candidates for this effect. Based on the published animal, human and epidemiological data, human chorionic gonadotropin (hCG), a glycoprotein hormone exclusively produced during pregnancy by the fetal part of placenta, has emerged as the most promising candidate[6;7]. The level of protection conferred by FTP may not be the same for all women, suggesting that there may be inherent variability in the protective effect across individuals. The hCG genes are well-known. Of the three trophoblastic hCG genes, hCGβ 5 is the most expressed gene in placenta, most highly conserved and the major contributor of hCG function during pregnancy [8;9]. The genotype of the fetal placenta is actually the genotype of the developing fetus. We proposed to examine the novel hypothesis that *the hCG genotype of a woman's offspring is associated with her breast cancer risk.* The data and biospecimens for this study are banked in the repository of the Metropolitan New York Registry (MNYR), one of six collaborating sites of the NCI funded Cooperative Family Registry for Breast Cancer Studies (CFRBCS). Since 1995, MNYR assembled 1,150 families with more than 3,500 individuals. Using the existing MNYR resources, a case-control study was designed to examine the hypothesis whether first-born offspring's hCGβ 5 genotype (i.e., placental hCGβ 5 genotype during first FTP) is associated with a woman's breast cancer risk. We proposed to evaluate our hypothesis by comparing the hCGβ 5 genotypes of first-born children of women with breast cancer (cases) and women without breast cancer (controls).

BODY:

This is the annul report for year 1 of the study. We have aimed to finish three tasks listed below during year 1 in the approved Statement of Work. To date, all three tasks have been accomplished. Questionnaire data on all participants are currently maintained in a relational database in Access which undergoes continuous quality-control checks. For the proposed study, a separate database specific for this project has been created containing all relevant data. Standard data cleaning and editing have been performed on these data to ensure that the case-control status, the relationship between the cases and controls and their first-born children, and the relevant risk factor information are accurate and consistent.

KEY RESEARCH ACCOMPLISHMENTS:

Year 1

Task 1: Identification of 1,106 eligible breast cancer cases and unaffected controls and their first-born children in MNYR database who are eligible for the study.
Task 2: Cleaning and editing of the questionnaire and family history data on the eligible study participants.
Task 3: Obtaining the DNA samples from the MNYR biospecimen bank on the 1,106 eligible study participants.

REPORTABLE OUTCOMES:

Not applicable

CONCLUSIONS:

We have accomplished the three tasks in the approved Statement of Work for year 1 as planned.

REFERENCES:

1. MacMahon B, Purde M, Cramer D, Hint E. Association of breast cancer risk with age at first and subsequent births: a study in the population of the Estonian Republic. J.Natl.Cancer Inst. 1982;69:1035-38.

2. Trichopoulos D, Hsieh CC, MacMahon B, Lin TM, Lowe CR, Mirra AP *et al.* Age at any birth and breast cancer risk. Int.J.Cancer 1983;31:701-04.

3. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol.Rev. 1993;15:36-47.

4. Rosner B, Colditz GA, Willett WC. Reproductive risk factors in a prospective study of breast cancer: the Nurses' Health Study. Am.J.Epidemiol. 1994;139:819-35.

5. Chie WC, Hsieh C, Newcomb PA, Longnecker MP, Mittendorf R, Greenberg ER *et al.* Age at any full-term pregnancy and breast cancer risk. Am.J.Epidemiol. 2000;151:715-22.

6. Russo IH, Russo J. Hormonal approach to breast cancer prevention. J.Cell.Biochem. 2000;34:1-6.

7. Rao ChV. Does full-term pregnancy at a young age protect women against breast cancer through HCG? Gynecol. 2000;96:783-86.

8. A.K.Miller-Lindholm, E.Bedows, C.F.Bartels, J.Ramey, V.Maclin, R.W.Ruddon, A naturally occurring genetic variant in the human chorionic gonadotropin-beta gene 5 is assembly inefficient. Endocrinology 140 (1999) 3496-3506.

9. A.K.Miller-Lindholm, C.J.LaBenz, J.Ramey, E.Bedows, R.W.Ruddon, Human chorionic gonadotropin-beta gene expression in first trimester placenta. Endocrinology 138 (1997) 5459-5465.

APPENDICES:

Not applicable